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## Early vs deferred highly active antiretroviral therapy in HIV infected infants: a European Collaborative Cohort Study

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### Background

Without antiretroviral therapy (ART), approximately 20% of HIV-1 vertically infected infants develop severe disease manifestations before the age of 1 year [1] and surrogate markers poorly predict infants at higher risk of rapid disease progression. Several small prospective and retrospective studies in developed countries have suggested that ART initiated early in life could prevent this rapid clinical and immunologic deterioration [2-6].

Because of the small number of HIV-infected infants delivered in industrialized countries where mother to child transmission prophylaxis is widely applied, a prospective study of early versus delayed ART is currently not feasible. Implementation of early ART has varied across countries and over time since 1996 in Europe. The objective of this collaborative study was to compare the out-

come of infants who received ART early in life with the outcome of those with deferred treatment.

### Materials and methods

Children born between 01/09/96 and 31/12/2004 to mothers with known HIV infection at birth, who received neonatal prophylaxis, and diagnosed with HIV before age 3 months were eligible. The children who were identified as HIV-infected at the same time or after being diagnosed with AIDS, and children who develop AIDS before the age of 3 months were excluded. Thirteen prospective and retrospective cohorts from 11 European countries participated, enrolling a total of 210 eligible infants. Data including general demographics and pregnancy data, details of prophylaxis and ART in early life, CDC events and death, immunological and virological measurements since birth, were collected and pooled. The risk of AIDS/death was estimated by Kaplan-Meier survival analysis,

and compared between the groups of infant treated or not treated before 3 months of age. Cox regression was used to estimate hazard ratios.

**Results**

Among the 210 children, 21 developed AIDS and 3 died. The exposure to treatment was heterogeneous among cohorts. Overall ART and Highly active ART were initiated in 59% and 48% of the infants before 3 months of age and in 87% and 76% by one year, respectively.

Treatment was initiated before the age of 3 months in 124 infants. There was no significant difference in demographic, pregnancy and delivery characteristics between the two groups. Moreover the proportion of infants with early treatment did not vary significantly over time. As shown in figure 1, we found that the risk of developing AIDS/death at one year was 1.6% in infants treated before the age of 3 months compared to 11.7% in infants who started treatment later (p<0.001). At 5 years the risks were 4.6% and 21.5% respectively. Deferred treatment was associated with a five-fold higher risk of AIDS has compared with treatment before 3 months of age (crude hazard ratio = 5.0; 95% CI: 2.0-12.6). Adjustment for ethnicity, birth weight, breast feeding, number and class of neonatal prophylaxis, number and class of drug in first treatment did not substantially affect the hazard ratio.

**Conclusion**

The preliminary results of this retrospective collaborative study suggest a significant association between ART

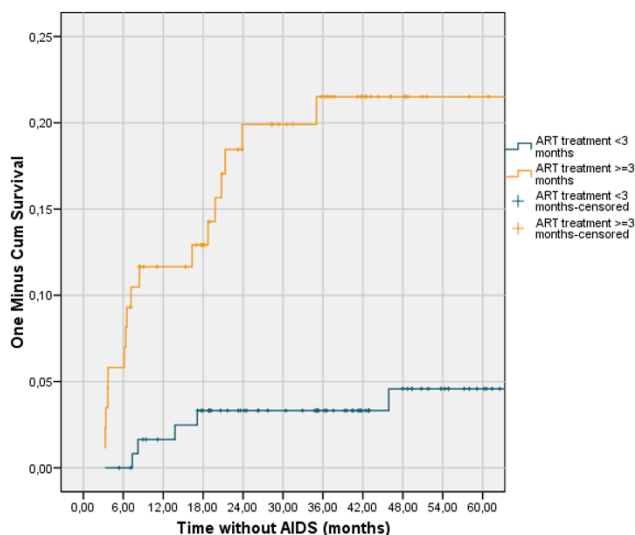
started before the age of 3 months and a lower subsequent incidence of AIDS/death in infancy.

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**Figure 1**  
Time from birth to AIDS/death comparing children treated before 3 months of age and children not treated before 3 months of age.

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